

Applicants: Leslie Lobel and Joyce Lustbader
Serial No.: 09/804,626
Filed: March 9, 2001
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REMARKS

Claims 1, 2, 4, 7, 16, 18, and 24-26 are pending. Claims 1, 2, 4, 7, 16, 25, and 26 have been amended to introduce certain format changes. Applicants submit that these amendments raise no issue of new matter. Thus, claims 1, 2, 4, 7, 16, 18, and 24-26 are still pending and under examination.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the December 5, 2003 Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

In particular, the Examiner stated that the host cell of claim 25 may produce a soluble polypeptide other than that encoded by the transfected vector and that the claim should be amended to indicate the identity of the soluble polypeptide being produced.

In response, applicants submit that claim 25, as amended, is clear and definite and respectfully request that the Examiner withdraw his rejection thereof.

Rejection Under 35 U.S.C. §103(a)

The Examiner rejected claims 1, 2, 4, 7, 16, 18, and 24-26 under 35 U.S.C. §103(a) as allegedly unpatentable over Hsueh in view of McCoy, of record.

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In response to the Examiner's rejection, applicants respectfully traverse, and maintain that the Examiner has failed to establish a *prima facie* case of obviousness.

The rejected claims provide, in relevant part, a nucleic acid which encodes a soluble polypeptide comprising an extracellular domain of a gonadotropin receptor and thioredoxin.

Hsueh teaches a fusion protein comprising the extracellular domain of, e.g., the LH receptor, wherein the extracellular domain of the receptor is linked to a transmembrane anchor protein.

McCoy teaches that heterologous genes encoding small peptides may be expressed in bacteria as fusion proteins comprising a "thioredoxin-like" protein, which fusion proteins are both soluble and stable relative to the peptides alone.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim. First, the cited references, when combined, teach or suggest every element of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Applicant maintains that the cited references fail to support a *prima facie* case of obviousness because one of skill would not have had a reasonable expectation of success in combining the teaching of Hsueh with that of McCoy to arrive at the claimed invention. Importantly, McCoy teaches the benefits of a thioredoxin fusion protein for stabilization and solubilization of small polypeptides, which due to problems

associated with their size are often poorly expressed in bacteria (see column 1 lines 25-30). The examples taught by McCoy comprise polypeptides of 14, 70, 114, 186, and 223 amino acids in length, corresponding to SEQ ID NOS:1-12, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, and SEQ ID NO:24, respectively. In contrast, the example given in the specification at page 54, lines 3-4, comprises a polypeptide that is 336 amino acids in length. Applicants maintain that one of skill would not have expected a thioredoxin fusion with such a large polypeptide to confer additional stability and solubility according to the teaching of McCoy, which demonstrated improved stability and solubility only for smaller polypeptides.

Furthermore, applicants submit that if McCoy had solved the problem of improved solubility and stability for all bacterially expressed proteins, the art would have been expected to produce the claimed gonadotropin receptor-thioredoxin fusion protein during the eight years following issuance of the McCoy patent. The fact is it did not, despite the need for improvements in the stability and solubility of recombinant gonadotropin receptor proteins that would enable the large-scale manufacture of the properly folded receptor, as noted in the specification at pages 2-3. Notably, this was an area of active research, as demonstrated by the Hsueh patent, which teaches an alternate solution to the problem of producing properly folded, soluble gonadotropin receptor proteins. In view of the continued need for recombinant gonadotropin hormone receptor that was both stable and soluble as well as subject to large-scale production, the failure of the art to teach or suggest combining the teachings of McCoy and Hsueh to arrive at the claimed invention demonstrates that such a combination was in fact not obvious to those of skill in the art.

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In view of the above remarks, applicants maintain that claims 1, 2, 4, 7, 16, 18, and 24-26 satisfy the requirements of 35 U.S.C. §103(a).

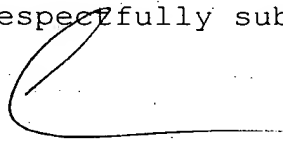
Summary

In view of the amendments and remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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2/27/03